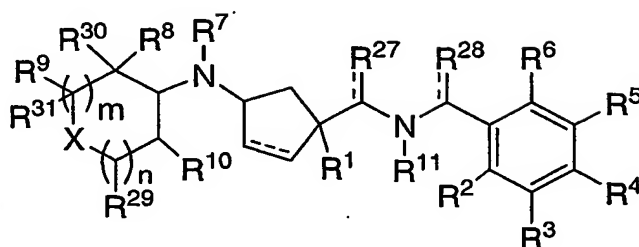


## WHAT IS CLAIMED IS:

1. A compound of the formula I:



I

wherein:

X is selected from the group consisting of:

-O-, -NR<sup>20</sup>-, -S-, -SO-, -SO<sub>2</sub>-, and -CR<sup>21</sup>R<sup>22</sup>-, -NSO<sub>2</sub>R<sup>20</sup>-,  
-NCOR<sup>20</sup>-, -NCO<sub>2</sub>R<sup>20</sup>-, -CR<sup>21</sup>CO<sub>2</sub>R<sup>20</sup>-, -CR<sup>21</sup>OCOR<sup>20</sup>-, -CO-, -O-C(CH<sub>3</sub>)<sub>2</sub>-O-,  
where R<sup>20</sup> is selected from: hydrogen, C<sub>1</sub>-6 alkyl, benzyl, phenyl,

C<sub>3</sub>-6 cycloalkyl where the alkyl, phenyl, benzyl, and cycloalkyl groups can be  
unsubstituted or substituted with 1-3 substituents where the substituents are  
independently selected from: halo, hydroxy, C<sub>1</sub>-3 alkyl, C<sub>1</sub>-3 alkoxy, -CO<sub>2</sub>H, -  
CO<sub>2</sub>-C<sub>1</sub>-6 alkyl, and trifluoromethyl,

where R<sup>21</sup> and R<sup>22</sup> are independently selected from: hydrogen, hydroxy,  
C<sub>1</sub>-6 alkyl, -O-C<sub>1</sub>-6 alkyl, benzyl, phenyl, C<sub>3</sub>-6 cycloalkyl where the alkyl, phenyl,  
benzyl, and cycloalkyl groups can be unsubstituted or substituted with 1-3  
substituents where the substituents are independently selected from: halo,  
hydroxy, C<sub>1</sub>-3 alkyl, C<sub>1</sub>-3 alkoxy, -CO<sub>2</sub>H, -CO<sub>2</sub>-C<sub>1</sub>-6 alkyl, and trifluoromethyl;

R<sup>1</sup> is selected from:

-C<sub>1</sub>-6 alkyl, -C<sub>0</sub>-6 alkyl-O-C<sub>1</sub>-6 alkyl, -C<sub>0</sub>-6 alkyl-S-C<sub>1</sub>-6 alkyl, -C<sub>0</sub>-6 alkyl-SO<sub>1-2</sub>-C<sub>1</sub>-  
6 alkyl, -C<sub>0</sub>-6 alkyl-SO<sub>2</sub>-NR<sup>26</sup>-C<sub>1</sub>-6 alkyl, -(C<sub>0</sub>-6 alkyl)-(C<sub>3</sub>-7 cycloalkyl)-(C<sub>0</sub>-  
6 alkyl), hydroxy, -CO<sub>2</sub>R<sup>20</sup>, heterocycle, -CN, -NR<sup>20</sup>R<sup>26</sup>, -NR<sup>26</sup>SO<sub>2</sub>R<sup>20</sup>, -  
NR<sup>26</sup>COR<sup>21</sup>, -OCOR<sup>20</sup>, and phenyl,

where R<sup>26</sup> is selected from: hydrogen, C<sub>1</sub>-6 alkyl, benzyl, phenyl, C<sub>3</sub>-6 cycloalkyl  
where the alkyl, phenyl, benzyl, and cycloalkyl groups can be unsubstituted or

substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, C<sub>1</sub>-3alkyl, C<sub>1</sub>-3alkoxy, -CO<sub>2</sub>H, -CO<sub>2</sub>-C<sub>1</sub>-6 alkyl, and trifluoromethyl

where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from: halo, hydroxy, -O-C<sub>1</sub>-3alkyl, trifluoromethyl, C<sub>1</sub>-3alkyl, -O-C<sub>1</sub>-3alkyl, -CO<sub>2</sub>R<sup>20</sup>, -SO<sub>2</sub>R<sup>20</sup>, -NHCOCH<sub>3</sub>, -NHSO<sub>2</sub>CH<sub>3</sub>, -heterocycle, =O, -CN,

and where the phenyl and heterocycle are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, C<sub>1</sub>-3alkyl, C<sub>1</sub>-3alkoxy and trifluoromethyl;

R<sup>2</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl;

15 R<sup>3</sup> is selected from: hydrogen, hydroxy, halo, C<sub>1</sub>-6alkyl, -O-C<sub>1</sub>-6alkyl, -NR<sup>20</sup>R<sup>21</sup>, -NR<sup>20</sup>CO<sub>2</sub>R<sup>21</sup>, -NR<sup>20</sup>CONR<sup>20</sup>R<sup>21</sup>, -NR<sup>20</sup>-SO<sub>2</sub>-NR<sup>20</sup>R<sup>21</sup>, -NR<sup>20</sup>-SO<sub>2</sub>-R<sup>21</sup>, heterocycle, -CN, -CONR<sup>20</sup>R<sup>21</sup>, -CO<sub>2</sub>R<sup>20</sup>, -NO<sub>2</sub>, -S-R<sup>20</sup>, -SO-R<sup>20</sup>, -SO<sub>2</sub>-R<sup>20</sup>, and -SO<sub>2</sub>-NR<sup>20</sup>R<sup>21</sup>;

20 R<sup>4</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl;

R<sup>5</sup> is selected from: C<sub>1</sub>-6alkyl substituted with 1-6 fluoro and optionally substituted with hydroxyl, -O-C<sub>1</sub>-6alkyl substituted with 1-6 fluoro, -CO-C<sub>1</sub>-6alkyl substituted with 1-6 fluoro, -S-C<sub>1</sub>-6alkyl, -pyridyl, fluoro, chloro, bromo, and phenyl;

R<sup>6</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl;

30 R<sup>7</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, and trifluoromethyl;

R<sup>8</sup> is selected from: hydrogen, C<sub>1</sub>-6alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro,

C<sub>1-3</sub>alkoxy, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, fluoro, -O-C<sub>1-3</sub>alkyl, where alkyl may be unsubstituted or substituted with 1-3 fluoro, and C<sub>3-6</sub> cycloalkyl, -O-C<sub>3-6</sub>cycloalkyl, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, -OCOR<sup>20</sup>, phenyl,  
 or R<sup>7</sup> and R<sup>8</sup> may be joined together via a C<sub>2-4</sub>alkyl or a  
 5 C<sub>0-2</sub>alkyl-O-C<sub>1-3</sub>alkyl chain to form a 5-7 membered ring;

R<sup>9</sup> is selected from: hydrogen, C<sub>1-6</sub>alkyl, where alkyl may be unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro, C<sub>1-3</sub>alkoxy, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, CO<sub>2</sub>R<sup>20</sup>, hydroxy, and -O-C<sub>1-6</sub>alkyl,  
 10 where alkyl may be unsubstituted or substituted with 1-6 substituents where the substituents are chosen from the group: fluoro, C<sub>1-3</sub>alkoxy, hydroxy, -CO<sub>2</sub>R<sup>20</sup>,  
 or R<sup>8</sup> and R<sup>9</sup> may be joined together by a C<sub>1-4</sub>alkyl chain or a  
 C<sub>0-3</sub>alkyl-O-C<sub>0-3</sub>alkyl chain to form a 3-6 membered ring;

15 R<sup>10</sup> is selected from: hydrogen, and C<sub>1-6</sub>alkyl, where alkyl may be unsubstituted or substituted with 1-6 fluoro, fluoro, -O-C<sub>3-6</sub>cycloalkyl, and -O-C<sub>1-3</sub>alkyl, where alkyl may be unsubstituted or substituted with 1-6 fluoro,

or R<sup>8</sup> and R<sup>10</sup> may be joined together by a C<sub>1-3</sub>alkyl chain or a single bond to

20 form a 3-6 membered ring; where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy,

or R<sup>8</sup> and R<sup>10</sup> may be joined together by a C<sub>1-2</sub>alkyl-O-C<sub>1-2</sub>alkyl chain to form a  
 25 6-8 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy,

or R<sup>8</sup> and R<sup>10</sup> may be joined together by a -O-C<sub>1-2</sub>alkyl-O- chain to form a 6-7  
 30 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -CO<sub>2</sub>R<sup>20</sup>, C<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkoxy;

R<sup>11</sup> is selected from: hydrogen, C<sub>1-6</sub>alkyl, and trifluoromethyl;

$R^{27}$  and  $R^{28}$  are independently selected from: =O, where  $R^{27}$ ,  $R^{28}$ , or both, is oxygen and is connected via a double bond, hydrogen, phenyl, and  $C_{1-6}$ alkyl which may be substituted or unsubstituted with 1-6 of the following substituents:  
-COR<sup>11</sup>, hydroxy, fluoro, chloro, -O- $C_{1-3}$ alkyl;

$R^{29}$ ,  $R^{30}$ , and  $R^{31}$  are independently selected from: hydrogen, methyl, hydroxyl, trifluoromethyl, methoxy, and trifluoromethoxy;

or  $R^{29}$  and  $R^9$  are connected by a  $C_{1-3}$ alkyl bridge;

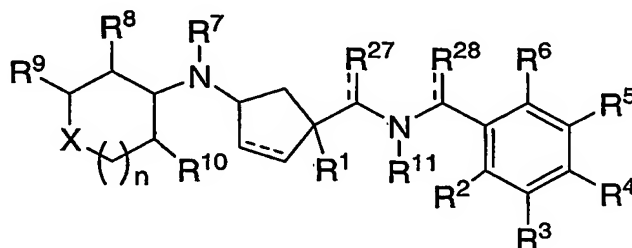
m is selected from 0, 1, and 2;

n is selected from 0, 1 and 2;

the dashed line represents a single or a double bond;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

2. The compound of Claim 1 of the formula Ia:



Ia

and pharmaceutically acceptable salts and individual diastereomers thereof.

3. The compound of Claim 1 wherein:

X is selected from the group consisting of: -O-, and -CH<sub>2</sub>-.

4. The compound of Claim 1 wherein X is -O-.

5. The compound of Claim 1 wherein  $R^1$  is selected from:

- (1) - $C_{1-6}$ alkyl, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, hydroxy, -O- $C_{1-3}$ alkyl, and trifluoromethyl,

- (2) -C<sub>0-6</sub>alkyl-O-C<sub>1-6</sub>alkyl-, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, and trifluoromethyl,
- (3) -C<sub>0-6</sub>alkyl-S-C<sub>1-6</sub>alkyl-, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from: halo, and trifluoromethyl,
- (4) -(C<sub>3-5</sub>cycloalkyl)-(C<sub>0-6</sub>alkyl), which is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from: halo, hydroxy, -O-C<sub>1-3</sub>alkyl, and trifluoromethyl.

6. The compound of Claim 1 wherein R<sup>1</sup> is C<sub>1-6</sub>alkyl which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from: hydroxy, and fluoro.

7. The compound of Claim 1 wherein:  
R<sup>1</sup> is selected from: isopropyl, -CH(OH)CH<sub>3</sub>, and -CH<sub>2</sub>CF<sub>3</sub>.

8. The compound of Claim 1 wherein:  
R<sup>2</sup> is selected from: hydrogen, hydroxy, trifluoromethyl.

9. The compound of Claim 1 wherein:  
R<sup>2</sup> is selected from: hydrogen, and hydroxy.

10. The compound of Claim 1 wherein:  
R<sup>3</sup> is selected from: C<sub>1-6</sub>alkyl unsubstituted or substituted with 1-6 fluoro, fluoro, chloro, bromo.

11. The compound of Claim 1 wherein:  
In the present invention it is more preferred that R<sup>3</sup> is selected from: trifluoromethyl, cyclopropyl, fluoro.

12. The compound of Claim 1 wherein:  
R<sup>5</sup> is selected from: C<sub>1-6</sub>alkyl unsubstituted or substituted with 1-6 fluoro, fluoro, chloro, bromo.

13. The compound of Claim 1 wherein:  
R<sup>5</sup> is selected from: trifluoromethyl, cyclopropyl, and fluoro.

5 14. The compound of Claim 1 wherein:  
R<sup>5</sup> is trifluoromethyl.

15. The compound of Claim 1 wherein R<sup>6</sup> is hydrogen.

10 16. The compound of Claim 1 wherein R<sup>7</sup> is hydrogen.

17. The compound of Claim 1 wherein R<sup>8</sup> is selected from: hydrogen, C<sub>1</sub>-  
3alkyl, which is unsubstituted or substituted with 1-6 fluoro, -O-C<sub>1</sub>-  
3alkyl, fluoro, and hydroxy.

15 18. The compound of Claim 1 wherein R<sup>8</sup> is selected from: hydrogen,  
methyl, ethyl, trifluoromethyl, fluoro, and -O-CH<sub>3</sub>.

19. The compound of Claim 1 wherein R<sup>9</sup> is hydrogen and R<sup>10</sup> is hydrogen.

20 20. The compound of Claim 1 wherein R<sup>8</sup> and R<sup>10</sup> are joined together by a -  
CH<sub>2</sub>CH<sub>2</sub>- chain or a -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>- chain to form a cyclopentyl ring or a cyclohexyl ring.

21. The compound of Claim 1 wherein R<sup>27</sup> is =O, where R<sup>27</sup> is  
25 oxygen and is connected via a double bond.

22. The compound of Claim 1 wherein R<sup>9</sup> and R<sup>29</sup> are joined together by a  
C<sub>1-3</sub>alkyl chain to form a ring.

23. The compound of Claim 1 wherein R<sup>29</sup> is hydrogen, R<sup>30</sup> is hydrogen, and  
30 R<sup>31</sup> is hydrogen.

24. A compound which is selected from the group consisting of the title compounds of the Examples, and pharmaceutically acceptable salts and individual diastereomers thereof.

25. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

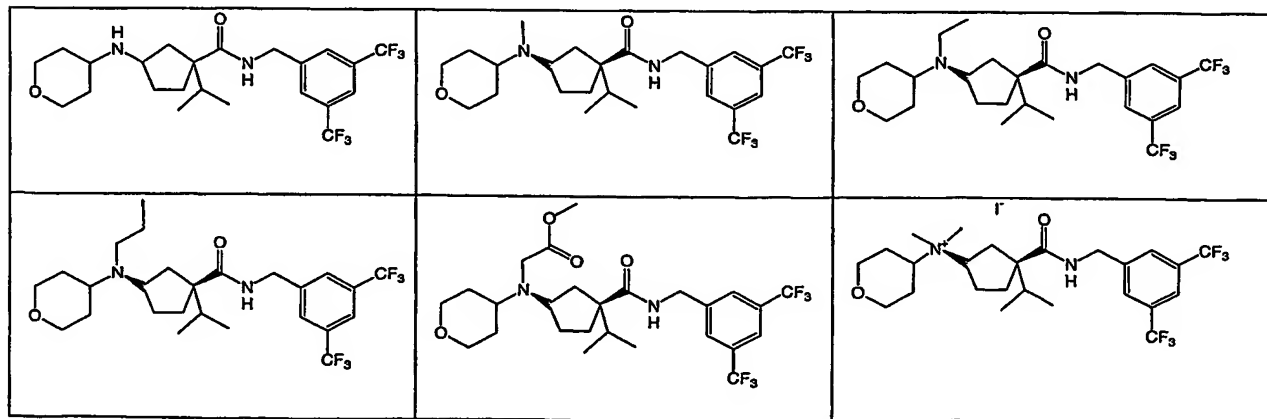
26. A method for modulation of chemokine receptor activity in a mammal in need thereof which comprises the administration of an effective amount of the compound of Claim 1.

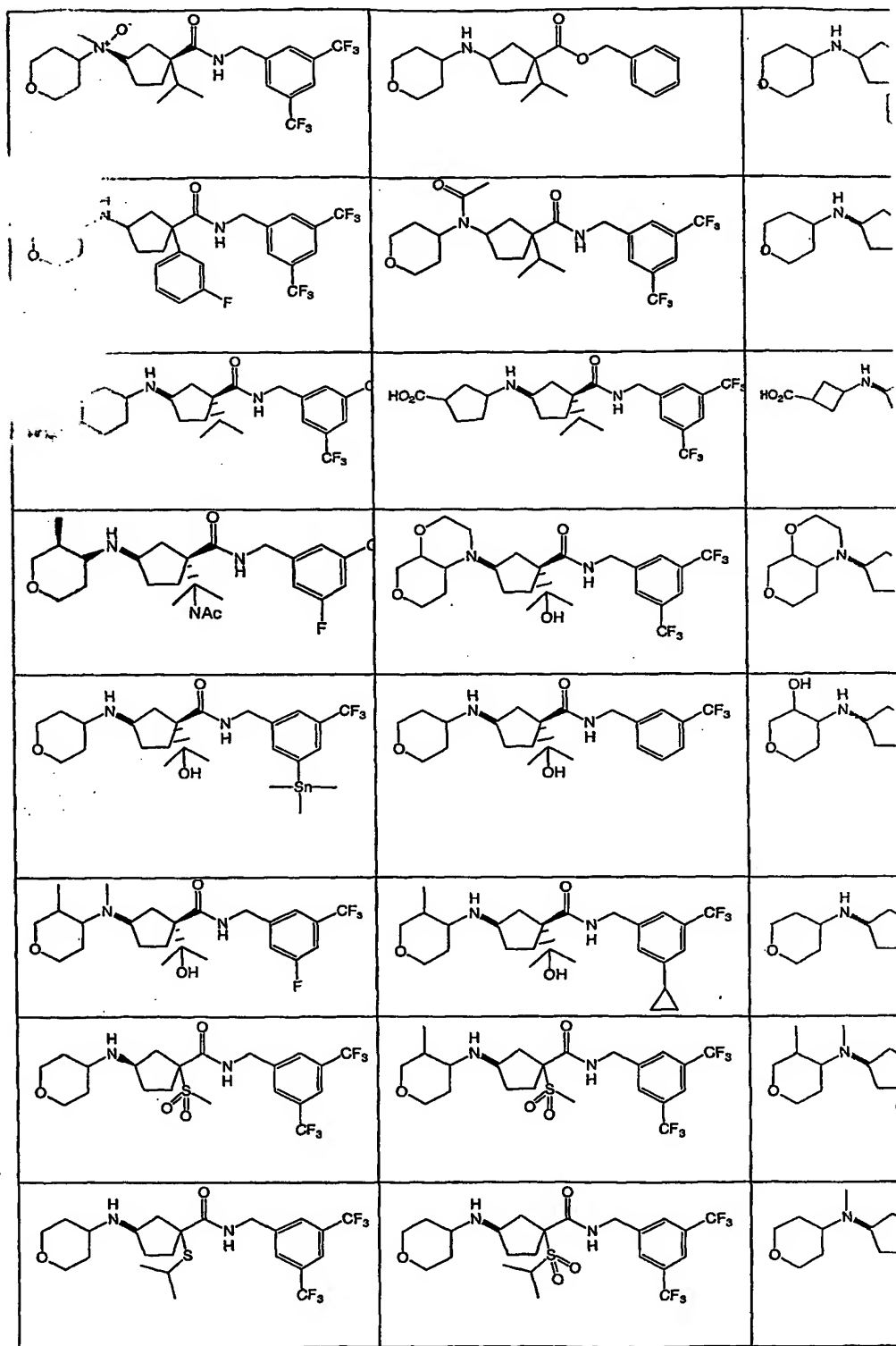
27. A method for treating, ameliorating or controlling an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

28. A method for reducing the risk of an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

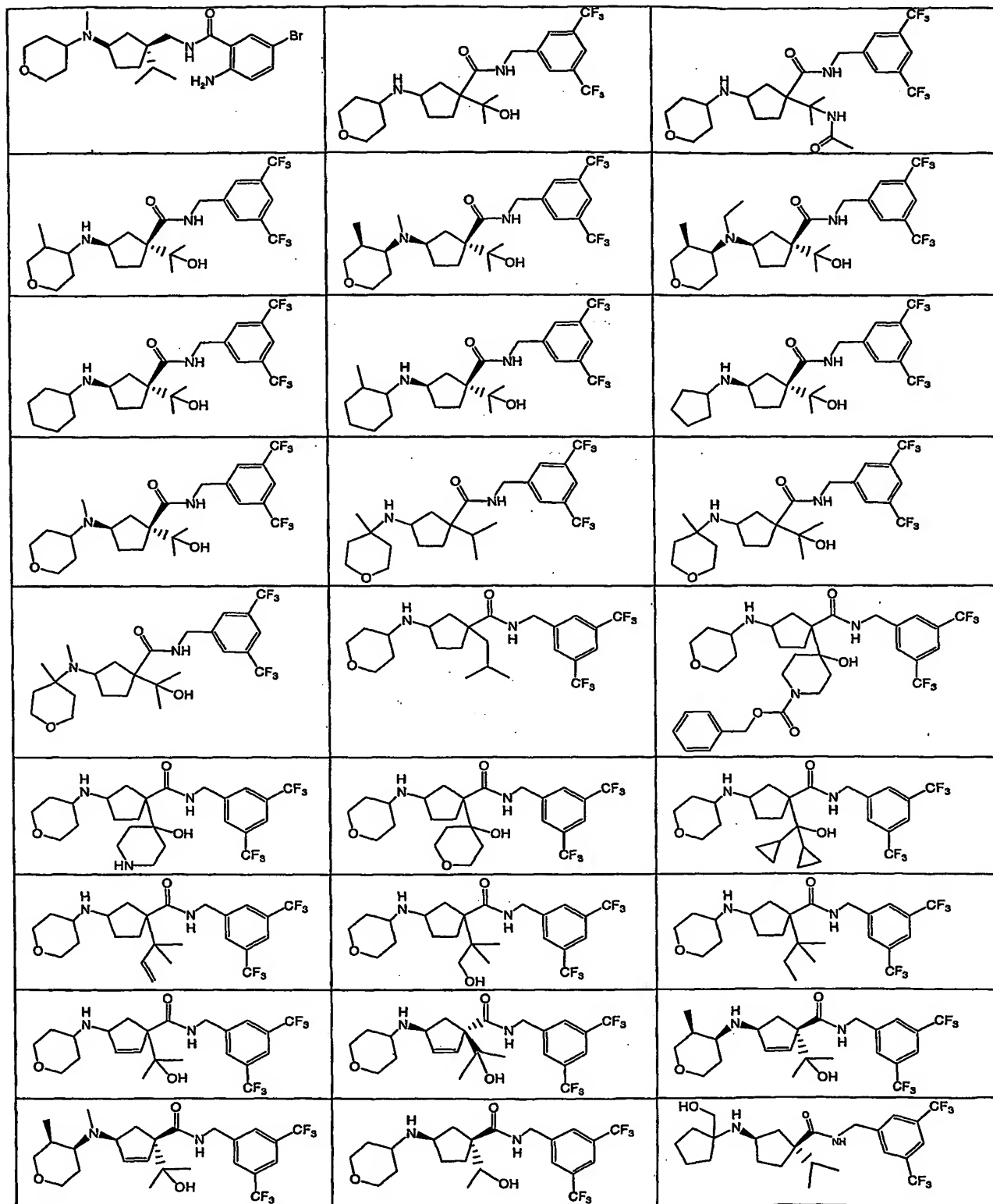
29. A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

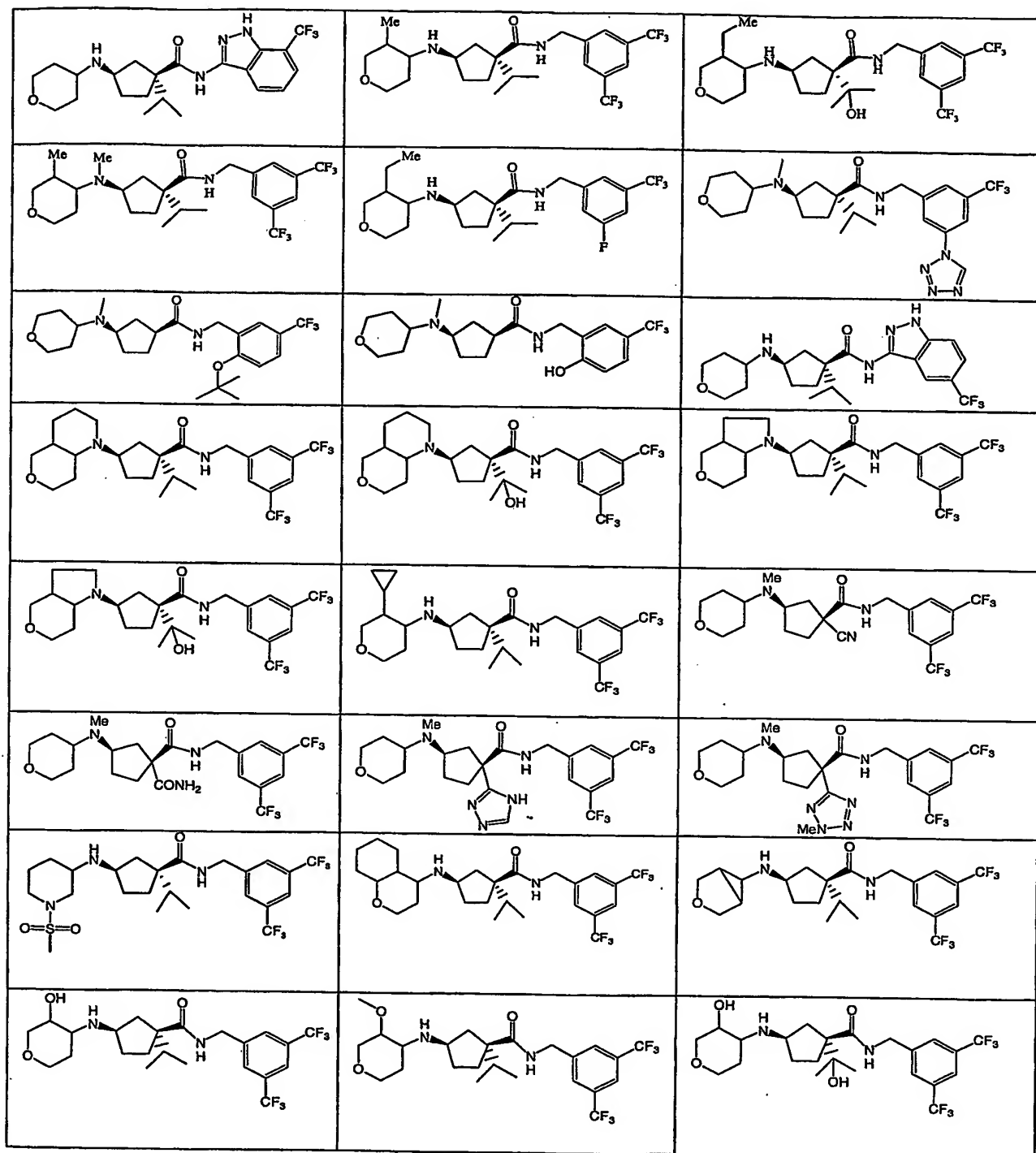
30. A compound which is selected from the group consisting of:

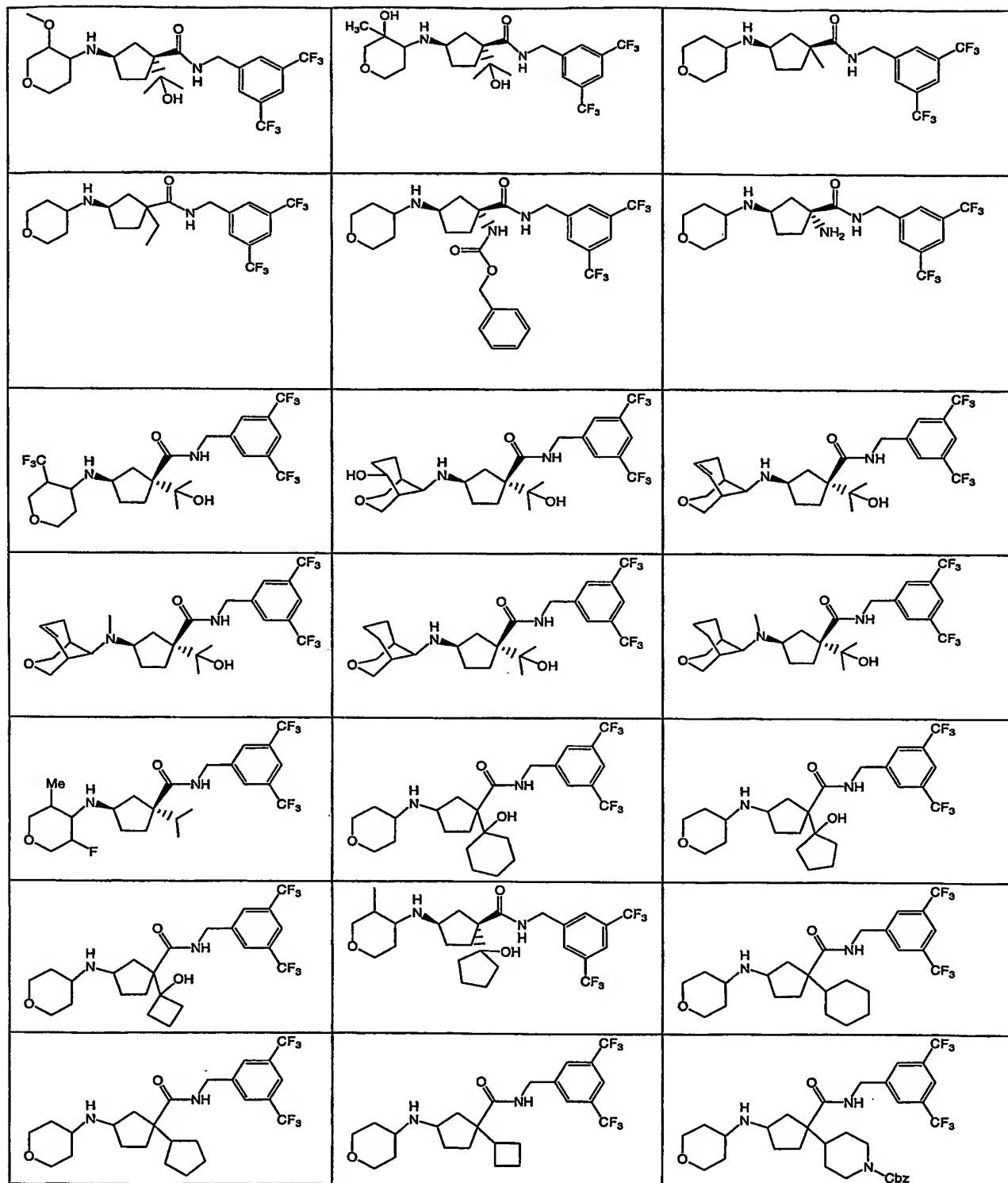


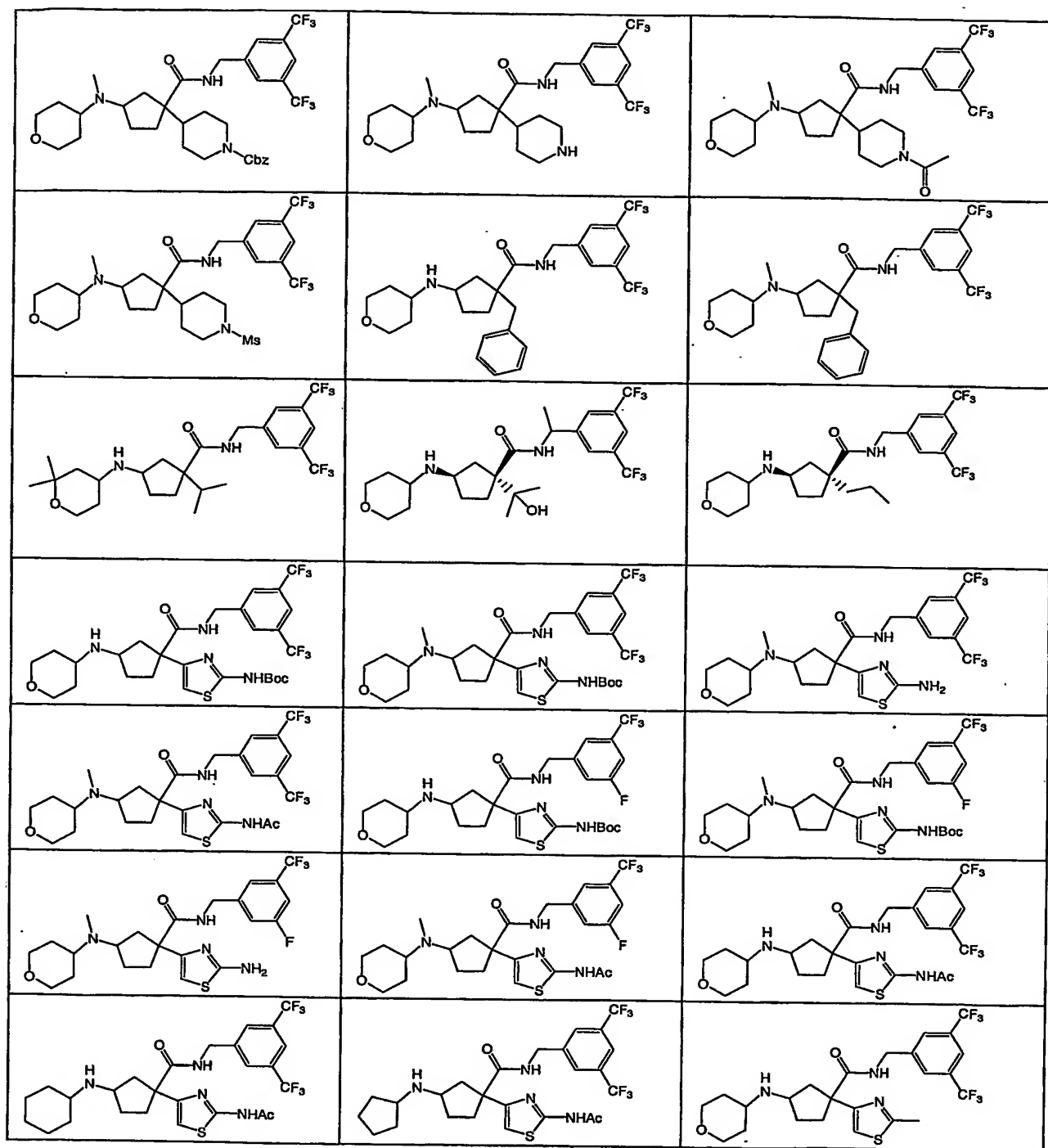


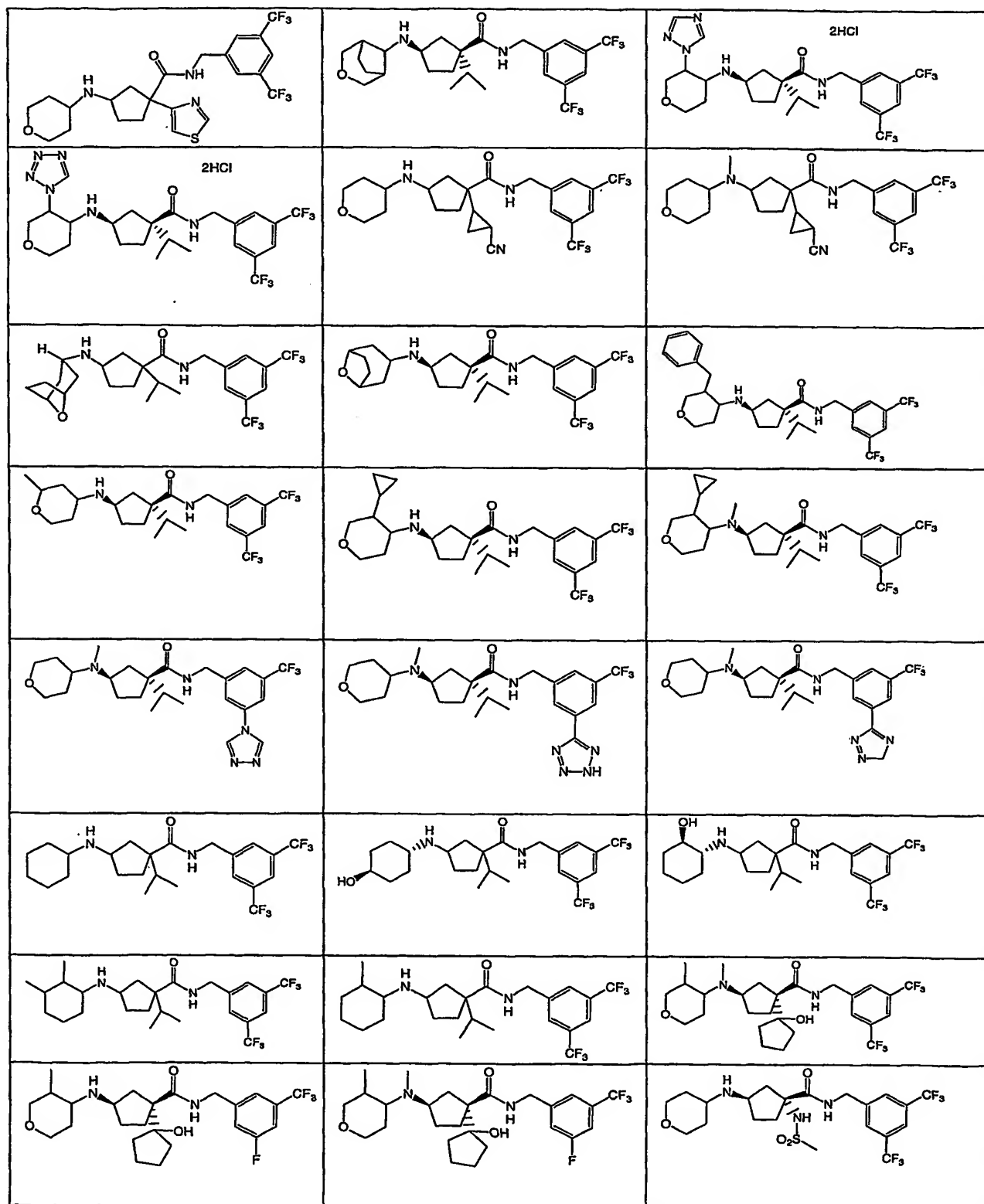


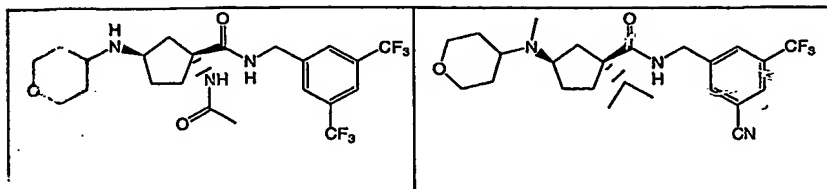






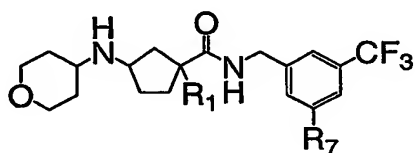






and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

31. A compound of the formula:

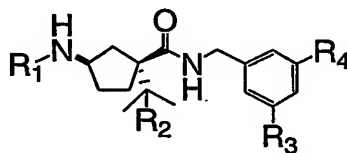


wherein  $R_7$  is F or  $CF_3$ , and wherein  $R_1$  is selected from:

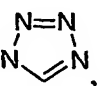

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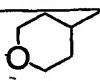
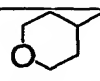

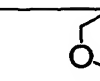

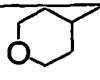
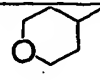

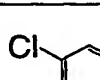




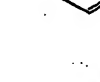

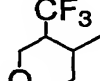
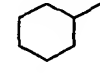

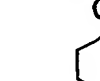

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

32. A compound of the formula:



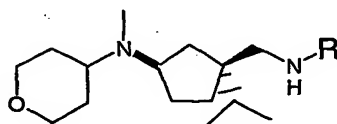
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wherein  $R_2$  is H or OH, wherein  $R_3$  is F or  $CF_3$ , wherein  $R_4$  is  $CF_3$ , Ph,  $OCF_3$ , Cl, or , and wherein  $R_1$  is selected from:

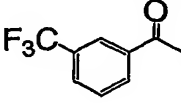
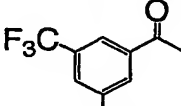
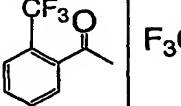
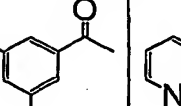
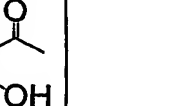
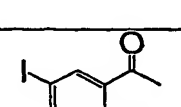
5 and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

33. A compound of the formula:



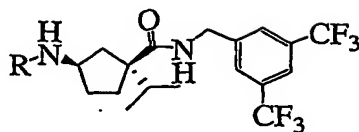
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wherein R is selected from:

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

34. A compound of the formula:



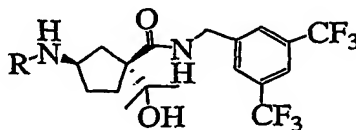
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wherein R is selected from:


and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

10

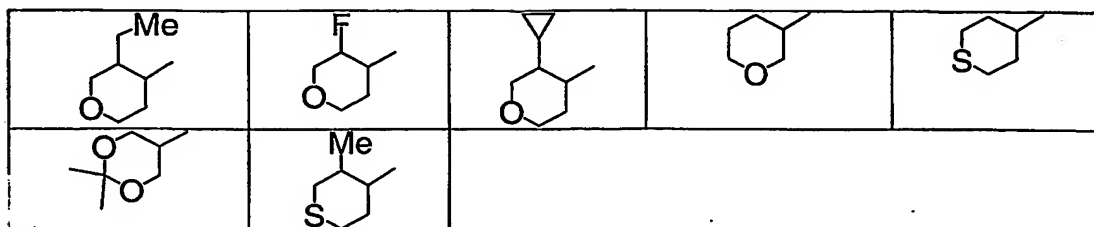
35. A compound of the formula:



wherein R is selected from:

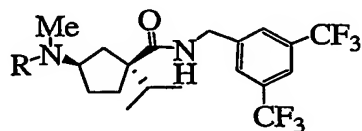
15



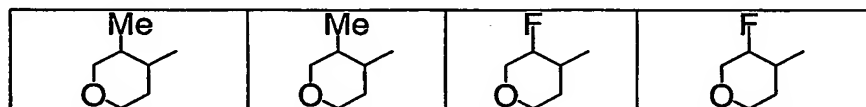


and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

36. A compound of the formula:



wherein R is selected from:



10

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.